REMARKS

I. Status of Claims

By virtue of the present Amendment, claims 3-5 and 8-10 have been canceled, without prejudice.

Claim 1 has been amended to specify that the active agent is co-spray dried with a force control agent which has hydrophobic moieties and is concentrated on the surfaces of the particles, and that the active agent is heparin and the force control agent is leucine. Claim 1 now reads:

> *A method of making a dry powder composition for pulmonary inhalation, the method comprising spray drying a pharmaceutically active agent in a spray dryer to produce active particles, wherein the step of spray drying further includes producing droplets moving at a controlled velocity, wherein the active agent is co-spray dried with a force control agent which has hydrophobic moieties, the force control agent being concentrated on the surface of the particles, wherein the active agent comprises heparin and the force control agent is leucine.*

Support for this amendment is as follows:

(i) the active agent is co-spray dried with a force control agent is found in Claim 6 of the application as filed;

(ii) the force control agent has hydrophobic moieties is found on Page 15 lines 1-2 of the application as filed; and

(iii) the force control agent being concentrated on the surfaces of the particles is found on Page 13, line 5-6 of the application as filed.

As a consequence of the amendments to claim 1, claims 8-10 have been cancelled. As noted above, Claims 3-5 have also been cancelled from the pending claims.

Claims 7 and 11-13 have been amended to correct the dependencies in view of the cancelled claims. Claim 14 has also been amended.

It is submitted that no new matter has been added by virtue of the present amendments.

II. Rejection under § 102(b) as anticipated by Snyder

In the Office Action, claims 1, 3-5 and 8-10 were rejected under 35 U.S.C. § 102(b) as anticipated by Snyder et al. (U.S. 2002/0071871)

Claim 1, as amended, is directed towards a method of making a dry powder formulation comprising an active and a force control agent, and requires that:

- the method comprises spray drying a pharmaceutically active agent to produce active particles;
- the sprayed droplets move at a controlled velocity;
- the active agent is co-spray dried with a force control agent;
- the force control agent has hydrophobic moieties;
- the force control agent is concentrated on the surfaces of the resulting particles; and
- the active agent is heparin and the force control agent is leucine.

The Snyder reference does not disclose a spray drying process in which the active agent is co-spray dried with a force control agent. Further, Snyder only teaches the coating of particles with a force control agent following spray drying in order to provide improved dispersibility. Snyder fails to teach co-spray drying an active with leucine, let alone co-spraying dry heparin with leucine as set forth in current claim 1. As a result, claim 1 cannot be anticipated by Snyder. Applicant points out that as claims 3-5 and claims 8-10 were cancelled in the present amendment, the Examiner's rejection of these claims are moot.

Reconsideration of the rejection is respectfully requested.

III. Rejection under § 103

A. Rejection under 35 U.S.C. § 103 over Snyder in view of Wiedmann

The Examiner rejected claims 1 and 2 of the present invention under 35 U.S.C. § 103 as being obvious over Snyder et al. in view of Wiedmann et al. (Pharm. Dev. & Tech.)

As amended, claim 1 requires that the active agent is co-spray dried with a force control agent, where the active agent is heparin and the force control agent is leucine; that the force control agent has hydrophobic moieties; and that the force control agent is concentrated on the surfaces of the resulting particles.

The Snyder reference purportedly teaches the coating of particles with a force control agent following spray drying in order to provide improved dispersibility. The Snyder reference fails to suggest or teach co-spray drying an active with a force control agent, and therefore cannot possibly teach or suggest co-spray drying an active with leucine, let alone co-spraying dry heparin with leucine.

The Wiedmann reference cannot cure the deficiencies of the Snyder reference as it also fails to teach or suggest co-spray drying an active with a force control agent. The Wiedmann reference further fails to teach or suggest that the active agent is heparin or the force control agent is leucine. As a result, the combination of the Snyder reference and the Wiedmann reference cannot render the present claims obvious.

Even were one of skill in the art to combine these references, one of skill would still not arrive at the claimed invention because these documents do not teach or suggest co-spray drying of an active with a force control agent.

Claims 1 and 2 are therefore not rendered obvious by the combination of the Snyder reference and the Wiedmann reference.

B. Rejection under 35 U.S.C. § 103 over Snyder in view of Kodas

The Examiner rejected claims 1, 6-7 and 26 under 35 U.S.C. § 103 as being obvious over Snyder et al. in view of Kodas (U.S. 6,051,257).

As amended, claim 1 requires that the active agent is co-spray dried with a force control agent, where the active agent is heparin and the force control agent is leucine; that the force control agent has hydrophobic moieties; and that the force control agent is concentrated on the surfaces of the resulting particles.

The Snyder reference purportedly teaches the coating of particles with a force control agent following spray drying in order to provide improved dispersibility. The Snyder reference fails to suggest or teach co-spray drying an active with a force control agent, and therefore cannot possibly teach or suggest co-spray drying an active with leucine, let alone co-spraying dry heparin with leucine.

The Kodas reference also fails to teach or suggest co-spray drying an active with a force control agent and also fails to teach or suggest a method wherein the active agent is co-spray dried with a force control agent, and wherein the active agent is heparin and the force control agent is leucine. As a result, it cannot cure the deficiency in the Snyder reference. Even were one of skill in the art to combine these references, one of skill would still not arrive at the claimed invention because these documents do not teach or suggest co-spray drying of an active with a force control agent.

Claims 1, 6-7 and 26 therefore are not rendered obvious in view of the combination of the Snyder reference and the Kodas reference.

C. Rejection under 35 U.S.C. § 103 over Snyder in view of Kuo

The Examiner has raised objections to claims 1, 8, and 11-15 as being obvious over Snyder in view of Kuo et al. (U.S. 6518239)

As amended, claim 1 requires that the active agent is co-spray dried with a force control agent, where the active agent is heparin and the force control agent is leucine; that the force control agent has hydrophobic moieties; and that the force control agent is concentrated on the

surfaces of the resulting particles. As noted above, claim 8 has been cancelled and therefore the rejection of this claim is rendered moot.

The Snyder reference purportedly teaches the coating of particles with a force control agent following spray drying in order to provide improved dispersibility. The Snyder reference fails to suggest or teach co-spray drying an active with a force control agent, and the force control agent of the Snyder reference is concentrated on the surfaces. The Snyder reference therefore cannot possibly teach or suggest co-spray drying an active with leucine, let alone co-spraying dry heparin with leucine.

The Kuo reference cannot cure the deficiencies of the Snyder reference as it neither discloses the step of spray drying to produce droplets moving at a controlled velocity nor the use of leucine. Further, the Kuo reference actually teaches away from using leucine by teaching spray-drying of an active with di-leucyl or tri-leucyl-containing peptides to increase the dispersibility of powdered compositions (and without using a means to control the velocity of particles). The Kuo reference indicates that the dispersibility of the di- and tri-leucyl containing powders is better than leucine in improving aerosol performance. The person skilled in the art would therefore have no motivation or reason to use leucine in a dry powder composition and would not consider co-spray drying an active with leucine, as taught in the present invention because the Kuo reference teaches that leucine alone does not provide improved aerosol performance.

The benefit conferred by the claims of the present invention is thought to be a result of the concentration of force control agent on the surface of the spray dried particles obtained by controlled velocity of the spray dried particles, which is reflected in an increase in fine particle fraction compared to the fine particle fraction of particles generated without controlled velocity. The manipulation or adjustment of the spray drying process is thought to result in a co-spray dried force control agent migrating to and concentrating on the surfaces of the particles which are produced. This means that the force control agent will be better able to reduce the tendency of the particles to agglomerate. Such surface concentration also is thought to assist in aerosolisation of the powder particles. The control of the spray drying process takes place

through production of droplets moving at a controlled velocity. In contrast, the method in the Kuo reference purportedly teaches the "uncontrolled" co-spray drying of actives with di- and tri-leucyl peptide to achieve increased dispersibility of the particles.

Claims 1 and 11-15 therefore are not rendered obvious by the Snyder reference in view of the Kuo reference.

D. Rejection under 35 U.S.C. § 103 over Snyder in view of Tarara

In the Office Action, the Examiner rejected claims 1, 25 and 27-29 under 35 U.S.C. § 103 as obvious over Snyder et al in view of Tarara et al. (U.S. 6,565,885)

As amended, claim 1 requires that the active agent is co-spray dried with a force control agent, where the active agent is heparin and the force control agent is leucine; that the force control agent has hydrophobic moieties; and that the force control agent is concentrated on the surfaces of the resulting particles.

The Snyder reference purportedly teaches the coating of particles with a force control agent following spray drying in order to provide improved dispersibility. The Snyder reference fails to suggest or teach co-spray drying an active with a force control agent, and therefore cannot possibly teach or suggest co-spray drying an active with leucine, let alone co-spraying dry heparin with leucine.

The Tarara reference cannot cure the deficiencies of the Snyder reference. The Tarara reference does not disclose or suggest the step of spray drying which includes producing droplets moving at a controlled velocity. Moreover, Tarara does not disclose heparin as an active agent or leucine as a force control agent. Claims 1, 25 and 27-29 therefore are not rendered obvious by the combination of the Snyder reference in view of the Tarara reference.

Further, the Tarara reference purportedly teaches how to produce low density perforated microstructures and also purportedly teaches that these particles have significantly reduced

attractive forces between them, and therefore better dispersibility. The Tarara reference therefore teaches an alternative solution to the problem of providing particles with improved dispersibility. Whereas the present invention teaches a method for producing particles with improved dispersibility by way of having force control agent concentrated on the surface of the particles, Tarara instead purportedly teaches that the same result can be achieved with perforated microparticles.

Both Snyder and Tarara provide alternative solutions to the problem of improving the dispersibility of particles. Therefore, the person skilled in the art would have no reason or motivation to combine the teachings of Snyder and Tarara.

For these further reasons, claims 1, 25 and 27-29 are not rendered obvious by the combination of the Snyder reference in view of the Tarara reference.

Even if the Snyder reference and the Tarara reference were combined, the person skilled in the art would not arrive at the claimed invention. The perforated microstructures disclosed in the Tarara reference are the result of the production process. Modification of the process steps disclosed in the Tarara reference, for example by spray drying the particles to produce droplets moving at a controlled velocity would potentially lead to a disruption in the process of the Tarara reference and to changes in the properties of the product. Further, the product of the Tarara reference is said to have better dispersibility because of the perforated microstructure. The person skilled in the art would have no incentive to take such structures and coat the particles, as purportedly taught by the Snyder reference as coating would clearly then affect the properties of such a perforated structure.

In view of the above, claims 1, 25 and 27-29 therefore are not rendered obvious by the Snyder reference in view of the Tarara reference.

In view of the foregoing, reconsideration and withdrawal of the rejections under 35 U.S.C. § 103 are respectfully requested.

Conclusion

This Response is being submitted in response to the Office Action dated December 2, 2009 in the above-identified application. Concurrently with this Response, Applicants submit a petition for three-month extension of time for filing a response, along with the requisite fee for a large entity. Therefore the time for filing a response to the Office Action dated December 2, 2009 is thereby extended to June 2, 2010. If it is determined that any additional fee is due in connection with this filing, the Commissioner is authorized to charge said fees to Deposit Account No. 50-0552.

An early and favorable action on the merits is earnestly requested.

Respectfully submitted,
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